IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF : Shin Hirayama et al.
SERIAL NUMBER : 10/616,921
FOR : HEALTH FOOD AND PREPARATION HAVING
AN ANTI-OBESITY EFFECT
FILED : November 3, 2003
GROUP ART UNIT : 1654
EXAMINER : COE, SUSAN D

DECLARATION UNDER 37 C.F.R. 1.132

Assistant Commissioner for patents

Washington, D.C. 20231

Sir,

I, Shin HIRAYAMA, a national of Japan, residing at 1-8-1, Sachiura,
Kanazawa-Ku, Yokohama, 236-0515, Japan, declares as follows

I have the following personal information.

Diploma

March 1987 University of TSUKUBA, the Master's Program in
Environmental Sciences

March 2000 Ph. D. of Agri., University of TSUKUBA

Occupation

April 1987 Mitsubishi Heavy Industries, Ltd., Advanced Technology
Research Center, Takasago Research & Development Center

November 1987 Employee of Mitsubishi Heavy Industries, Ltd., Advanced
Technology Research Center

April 2004 Research Manager of Mitsubishi Heavy Industries, Ltd.,
Advanced Technology Research Center

I am a co-applicant of the above-identified application.

When I conducted the experiment described in Experiment 2 of the present application I confirmed the following facts:

When the sea lettuce administrated group and the control group (non-administrated group) were fed with sea lettuce powder at an average of 22g/day during the administration period, both groups ate the same amount of foods.

Therefore, the diet effect of the present invention does not result from the appetite suppression effect.

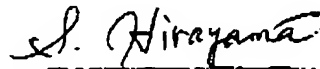
After confirming that the rats administrated with a crude D-cysteinoic acid extract ate the total amount of food, the food efficiency (weight increase/food intake) was measured. The food efficiency was 0.33 in the group administrated with no extract, 0.30 in the group administrated with 3.5% extract, and 0.31 in the group administrated with 7% extract.

In other words, the food efficiency tends to be lower in the groups administrated with the crude D-cysteinoic acid extract. If the groups administrated with the crude D-cysteinoic acid extract are fed with the same amount of foods, they can hardly increase their weight. In other words, the effect of the present invention does not result from the suppression of appetite caused by reducing the amount of foods supplied to the groups administrated with the crude D-cysteinoic acid extract.

I, the undersigned, declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Date

17th Mar 2005



Shin HIRAYAMA



In re Shetty

(CCPA)

195 USPQ 753

Decided Nov. 17, 1977

No. 77-515

U.S. Court of Customs and Patent Appeals

Headnotes

PATENTS

1. Patentability -- Invention -- Specific cases -- Chemical (§ 51.5093)

It is obvious and there is sufficient motivation to person skilled in chemical or pharmaceutical arts to substitute ethylene link between adamantane ring and amine for structurally-similar prior art methylene link.

2. Patentability -- Invention -- In general (§ 51.501)

Patentability -- Invention -- Specific cases -- Chemical (§ 51.5093)

Fact that claimed method might be inherent in teachings of prior art is immaterial if one of ordinary skill in art would not appreciate or recognize that inherent method; mere hindsight assertion that corresponding dosages of prior art compounds useful for combatting microbial infestation, in light of which claimed compound is obvious, renders claimed method for appetite control obvious is untenable; inherency of advantage and its obviousness are entirely different questions; obviousness cannot be predicated on what is unknown.

Particular patents -- Adamantane Derivatives

Shetty, Anorectic Adamantane Derivatives and Method of Using Same, rejection of claim 52 affirmed; rejection of claims 2-5 and 51 reversed.

Case History and Disposition:

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Appeal from Patent and Trademark Office Board of Appeals.

Application for patent of Bola Vithal Shetty, Serial No. 171,736, filed Aug. 13, 1971. From decision rejecting claims 2-5, 51, and 52, applicant appeals. Modified.

Attorneys:

Carl A. Hechmer, Jr., and Edward A. Sager, both of Philadelphia, Pa., for appellant.

Joseph F. Nakamura (Jack E. Armore, of counsel) for Commissioner of Patents and Trademarks.

Judge:

Before Markey, Chief Judge, Rich, Baldwin, and Lane, Associate Judges, and Morgan Ford, Associate Judge, United States Customs Court.

Opinion Text**Opinion By:**

Rich, Judge.

This appeal is from that portion of the July 30, 1976, decision of the Patent and Trademark Office (PTO) Board of Appeals (board) rejecting claims 2-5, 51, and 52 in application serial No. 171,736, filed August 13, 1971, entitled "Anorectic Adamantane Derivatives and Method of Using Same." The board rejected the claims under 35 USC 103 on new grounds, as provided in 37 CFR 1.196(b), as obvious from Brake ¹ in view of Narayanan, ² Bernstein et al., ³ and Bernstein. ⁴ We affirm the rejection of composition claim 52 and reverse the rejection of method claims 51 and 2-5.

The Invention

The invention pertains to a method, as defined in claims 51 and 2-5, of curbing appetite in animals by administering certain adamantane compounds. ⁵ The invention also pertains to the unit dosage form of a composition for curbing appetite comprising such an adamantane compound and a pharmaceutically acceptable carrier as defined in claim 52.

In the specification, appellant identifies his claimed compounds as follows:

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or their pharmaceutically acceptable acid addition salts, wherein:

R₁ = H, lower alkyl, aralkyl, aralkyl substituted with NH₂, OH, OCH₃, halogen, alkyl, NO₂; phenoxyalkyl or phenoxyalkyl substituted with NH₂, OH, OCH₃, halogen, alkyl, or NO₂; acyl such as formyl or acetyl.

R₂ = H, lower alkyl, COO-lower alkyl, aralkyl, aralkyl substituted with NH₂, OH, OCH₃, halogen, alkyl, NO₂; phenoxyalkyl or phenoxyalkyl substituted with NH₂, OH, OCH₃, halogen, alkyl, or NO₂; acyl such as formyl or acetyl.

R₁ and R₂ can be joined together to form, with the nitrogen, a heterocyclic ring (e.g. *Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.*)

R₃ = H, lower alkyl, or alkynyl

R₄ = H, lower alkyl, or alkynyl

R₅ = H, OH, halogen, or lower alkyl

R₆ = H, OH, halogen, or lower alkyl

R₅ and R₆ together may represent a carbonyl oxygen

R₇ = H, lower alkyl, halogen, hydroxy, alkoxy, amino or substituted amino, trifluoromethyl, sulfamyl, nitro, phenyl

R₈, R₉, R₁₀, R₁₁, R₁₂ are any of R₇

n = 0 to 4

m = 0 to 4

Independent claim 51 defines the "method of curbing appetite in an animal which comprises administering to the animal an amount effective to curb appetite of a compound" of the above formula.

The References

Brake describes a process for improving the yield of α -methyl multicyclic methylamines, one of which is α -methyl-1-adamantanemethylamine, illustrated as: *Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.*

where R is * * *:

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and is described as being useful as an antiviral agent in animals.

Narayanan teaches adamantyl sulfonamide compounds, useful as antimicrobial agents, e.g., as antiviral agents, of the formula:

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wherein R and R₁ each is hydrogen, halogen, lower alkyl, phenyl or phenyl-lower alkyl, R₂ is hydrogen or lower alkyl, R₃ is hydrogen, lower alkyl, lower alkoxy, halogen or halo-lower alkyl and n is 0, 1 or 2, and salts thereof.

Narayanan also teaches the use of his compounds in dosages corresponding to those of appellant.

Bernstein et al. pertains to adamantyl biguanides of the formula:

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and to acid-addition salts thereof.

In Formula I, R and R₁ each is hydrogen, halogen, lower alkyl, phenyl or lower alkoxy, R₂, R₃ and R₄ each is hydrogen, lower alkyl or phenyl-lower alkyl and n is 0 or 1.

These compounds are hypoglycemic agents effective in reducing blood sugar content in mammals.

The compounds of the Bernstein patent are illustrated by the following formula:

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and to acid-addition and quaternary ammonium salts thereof.

These compounds are adamantyl derivatives of phenothiazines, therapeutically active as central nervous system depressants.

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The Rejection

The examiner rejected appellant's claimed composition and method as obvious under 35 USC 103 in view of the teaching in Brake of administering to animals structurally similar adamantane derivatives "analogous" to those claimed. The Bernstein and Narayanan patents were cited to show similar compounds in the art. The examiner reasoned that the composition claim would have been obvious from the prior art because the respective compounds differ merely by a methylene group, i.e., the instant compounds have at least an ethylene link between the adamantane ring and the amine, whereas the prior art compound has a methylene link. This "minor molecular modification" was further asserted to be made obvious by the Bernstein and Narayanan patents, which disclose lower alkylene links between adamantane and other moieties and are directed to pharmaceutical uses.

The board treated the examiner's rejection as relying upon Brake alone and as citing the Bernstein and Narayanan patents to show the state of the art. The board did not sustain the rejection of claims 2-5, 51, and 52 as obvious from Brake alone because Brake's failure to disclose an amount of his compound effective as an antiviral agent

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renders unobvious the administration of "adjacent homologs of Brake's compound 'in an amount effective to curb appetite' * * *." Similarly, the board did not agree that appellant's composition in an "appetite curbing amount" would have been obvious from Brake alone.

Under 37 CFR 1.196(b), the board made a new ground of rejection under 35 USC 103 for obviousness from Brake in view of the Bernstein and Narayanan patents. The board agreed with the examiner that appellant's compounds having an ethylene linkage would have been obvious in view of Brake's corresponding adjacent homolog (methylene linkage). Relative to the method claims, the board found sufficient motivation in the prior art to administer Brake's compound and adjacent ethylene "homologs" as antiviral agents, and concluded that administering appellant's compounds in appetite-curbing amounts would have been obvious from Brake and Narayanan since the amounts suggested by Narayanan to achieve antiviral effects encompass the amounts intended and claimed by appellant.

The Arguments

Appellant contends that, after refusing to sustain the examiner's rejection on the basis of Brake alone, the board erred in rejecting the method claims by considering Narayanan in addition to Brake. Appellant argues that Narayanan's reference to dosage for treating viral infection is an improper basis for rejection. It is urged that the board mistakenly assumed that appetite-suppressant effects of appellant's compounds would be readily recognized from treating virus-infected animals with a related compound. It is also urged that the board ignored differences in treatments for viral infection and obesity, and that therefore Narayanan's dosage cannot be said to result in effective anorexia. Relative to the claimed composition, appellant states that there is an appreciable difference between the structure of the compounds of the claim and the prior art compounds, and that the former would not have been obvious because the motivation to make the required structural variation is absent.

The solicitor responds by arguing that in the absence of comparative evidence of any unexpected difference in the properties of appellant's and Brake's compounds, the compounds of the claim would have been obvious from and unpatentable over the structurally closely related compound disclosed by Brake. It is argued that Brake and Narayanan render obvious appellant's pharmaceutical carrier and "unit dosage form." As to the method claims, the solicitor contends that Narayanan discloses adamantyl compounds as antiviral agents in dosages that correspond to and would suggest similar and inherently appetite-curbing amounts of the Brake antiviral compound. The solicitor supports the board position that because appellant's compounds are homologous and there is sufficient motivation in the prior art to administer Brake's compound as an antiviral agent, appellant's different purpose does not render the method claims unobvious.

Opinion

We note at the outset that the ethylene linkage of appellant's compound closest to the prior art (β -(1-adamantyl)- α -methylethylamine) is referred to by the examiner as "analogous" to the methylene linkage of Brake's α -methyl-1-adamantanemethylamine and by the board as a "homolog." Since the appellant has not challenged either of these classifications, we proceed on the assumption that he accepts the inference that his compounds, whether homologs or analogs, would be expected to have similar properties

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to the prior art compound. Whether the adamantyl compounds in question are properly classified according

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to the usual definitions of "homolog" and "analog," we shall not consider inasmuch as appellant has not argued the point.

The solicitor has taken the position that absent comparative evidence demonstrating any unexpected difference in the properties of the compounds, the claimed composition would have been obvious from and unpatentable over the structurally closely related compound disclosed in Brake. On the other hand, appellant contends that the presence of the ethylene rather than the methylene group constitutes "an appreciable difference in the claimed compound and the prior art compounds," and relies on *In re Taborsky*, 502 F.2d 775, 183 USPQ 50 (CCPA 1974) for support of his argument that without some teaching of motivation to make the required molecular variation, a finding of obviousness based on structural similarity is improper.

[1]Regarding this issue of structural similarity, we agree with the solicitor and the PTO position. The examiner noted the difference of a mere methylene group between the compound of the claim and the prior art compounds, cited the Bernstein and Narayanan references showing the state of the art as prior art knowledge of use of lower alkylene links between adamantane and other moieties, and concluded that "this minor molecular modification would clearly be obvious to the pharmaceutical chemist." We do not accept appellant's contention that the adjacent alkylene link in question constitutes an "appreciable difference" in the compounds. We think that a person skilled in chemical and/or pharmaceutical arts would not hesitate to extend the alkylene linkage of the prior art compound. Further, we note that appellant's compound closest to the prior art and its synthetic preparation are disclosed in Narayanan as one of a group of compounds for producing his adamantyl sulfonamide. This leaves no room for doubt that the prior art knowledge renders appellant's compound structurally similar and provides sufficient motivation to make it.

Moreover, appellant has no basis for relying on *Taborsky*, supra. Unlike the present case, the prior art of record in *Taborsky* expressly limited the scope of "halogen" to exclude appellant's claimed fluorosalicylanilide compounds and stated "'several disadvantages in practice'" of free salicylanilides. 502 F.2d at 781, 183 USPQ at 55 (emphasis supplied). Appellant here has shown no such reason to preclude the conclusion that appellant's compounds are structurally similar to the prior art compounds.

Confronted with PTO evidence of obviousness, appellant has offered no evidence of unobviousness, as by showing an actual difference in properties between his compounds and the prior art compounds. In *re Hoch*, 57 CCPA 1292, 428 F.2d 1341, 166 USPQ 406 (1970). Appellant merely shows that his novel compounds are appetite suppressants whereas the reference compounds are not so known. Further, appellant has not indicated whether his compounds are antiviral, as is Brake's prior art compound. Presented with such an absence of comparative or other evidence with respect to the properties of the compounds and the claimed composition, we hold that composition claim 52 would have been obvious from and unpatentable over the prior art.

[2]Regarding method claims 51 and 2-5, the solicitor agrees with the board that:
* * * the compounds of claim 51 are obvious from and unpatentable over the corresponding Brake compound and the Narayanan disclosure of a dosage which *corresponds* to appellant's disclosed appetite curbing dosage (therefore, *inherently* appetite curbing). [Emphasis added.]

We cannot accept this conclusion. The issue here is whether the claimed method of curbing appetite would have been obvious. That appellant's "amount effective to curb appetite" corresponds to or inheres in Narayanan's amount "to combat microbial infestation" does not persuade us of the obviousness of appellant's method. As this court said in *In re Naylor*, 54 CCPA 902, 905-06, 369 F.2d 765, 768, 152 USPQ 106, 108 (1966):

[Inherency] is quite immaterial if, as the record establishes here, one of ordinary skill in the art would not appreciate or recognize that inherent result. * * *

* * * we find nothing in the record which would afford one of ordinary skill reason to anticipate that a trial * * * [of the combined prior art teachings] would be successful in producing the polymer recited in the claims.

The Patent Office has failed to show a reasonable expectation, or some predictability, that Brake's compound would be an effective appetite suppressant if administered in the dosage disclosed by Narayanan. The mere hindsight assertion that corresponding dosages render appellant's method obvious is untenable.

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Prior to appellant's disclosure, none of the adamantane compounds in any of the references before us suggested a use, much less a dosage, for curbing appetite. What we said in *In re Spormann*, 53 CCPA 1375, 1380, 363 F.2d 444, 448, 150 USPQ 449, 452 (1966), relative to inherency applies equally here:

As we pointed out in *In re Adams*, 53 CCPA 996, 356 F.2d 998, 148 USPQ 742 [(1966)], the inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.

Accordingly, the decision of the board is *affirmed* as to claim 52 and *reversed* as to claims 51 and 2-5.

Footnotes

Footnote 1. U.S. Patent No. 3,489,802, issued Jan. 13, 1970, on application serial No. 610,779, filed Jan. 23, 1967.

Footnote 2. U.S. Patent No. 3,501,511, issued Mar. 17, 1970, on application serial No. 661,781, filed Aug. 21, 1967.

Footnote 3. U.S. Patent No. 3,270,036, issued Aug. 30, 1966, on application serial No. 493,899, filed Oct. 7, 1965.

Footnote 4. U.S. Patent No. 3,320,249, issued May 16, 1967, on application serial No. 470,930, filed July 9, 1965.

Footnote 5. Adamantane is the trivial name assigned to tricyclodecane. Its structural

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formula can be represented in any of the following ways:

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- End of Case -

